

**REMARKS**

Claims 1, 3-17, 27 and 31-37 are pending in the present application. Claim 11 has been amended so that it now depends on claim 10 instead of on claim 9.

Applicants have carefully considered the final Office Action mailed on March 31, 2009 and the Advisory Action mailed on July 2, 2009 and respond to the specific issues raised therein as follows:

***Claim Rejections – 35 USC § 103***

Claims 1-17 and 27 have been rejected under 35 U.S.C. 103(a) as being unpatentable over the article titled “*Macromolecular Chemistry and Physics*” by Penco et al. (“Penco”) in view of U.S. Patent Application Publication No. US 2001/0009662 to Cohn et al. (“Cohn”).

Penco discloses multi-block copolymers containing two different biodegradable polyester segments. One of the pre-polymers --poly( $\epsilon$ -caprolactone)-- is provided with reactive groups at both ends --poly( $\epsilon$ -caprolactone) diol terminated (PVDT)-- which react with the other pre-polymer --poly(lactic-glycolic acid) (PLGA)-- to form alternating multi-block copolymers. *See* e.g., page 1744, under item 1 of Conclusions.

Cohn discloses polymeric compositions comprising the reaction product of a diol, diamine or dicarboxylic acid with a chain extender or coupling agent in about a 1:2 mole ratio. The resulting product is reacted with a monofunctional hydroxyl, amine or carboxylic acid containing compound to produce a pentamer. Cohn teaches the synthesis of multi-block

copolymers having a controlled block distribution by using ACA blocks and a monofunctional block AB. This exclusively results in alternating block copolymers having uniform length.

The claims for the present invention require multiblock copolymers wherein the segments of the copolymer are linked by an aliphatic chain-extender and randomly distributed in the copolymer. The specification discloses at page 12, lines 5-11 that:

The method to obtain a copolymer with a random distribution of a and b (and optionally c) is far more advantageous than when the segments are alternating in the copolymer such as in (ab)<sub>n</sub> with the ratio of prepolymers a and b being 1. The composition of the copolymer can then only be determined by adjusting the pre-polymer lengths. In general, the a and b segment lengths in (ab)<sub>n</sub> alternating copolymers are smaller than blocks in block-copolymers with structures ABA or AB.

Penco does not teach or suggest block copolymers linked by an aliphatic chain-extender. Penco teaches the preparation of multi-block copolymers containing segments of PLGA coupled with segments of poly(ε-caprolactone)s (PEG) by a “chain extension process using as diols α,ω-bishydroxy-terminated oligomers of caprolactone of different molecular weight.” However, there is no teaching or suggestion by Penco of a separate PEG chain extender. Instead, Penco teaches that the segments are functionalized in such a way that the segments can directly react with each other to form a block copolymer.

In support of their position that Penco does not teach or suggest the randomly segmented multiblock copolymers in the claims, the Applicants are submitting herewith a Declaration by Dr. Theodorus Adrianus Cornelis Flipsen, one of the inventors. Dr. Flipsen explains that the Applicants’ multiblock copolymers with randomly distributed segments are significantly

different than “the copolymer taught by Penco [which] has segments A and B that are distributed in alternating form.” Flipsen Declaration, ¶ 11; see also ¶¶ 8-12.

Dr. Flipsen also explains how the block copolymers taught by Cohn have very specific structures and how Cohn does not teach or suggest multi-functional prepolymers that are chain extended in a statistical, random manner as required by the claims. Flipsen Declaration, ¶¶ 13-16.

The third paragraph of the section titled, “Response to Arguments,” on page 9 of the Office Action states that:

Penco *et al.* further teaches on page 1740 (*Molecular Characteristics*), that the PLGA-PCDT block copolymer samples had different compositions of the PLGA blocks as well as different lengths of the PCDT blocks. Thus, since the PLGA oligomers may differ in their composition (e.g. mole ratio of LA/GA), it follows that Penco, suggests that different polymers of PLGA can reside within the same PLGA-PCDT copolymer.

Dr. Flipsen explains that although Penco teaches different PLGA oligomers, there is no teaching or suggestion of different PLGA oligomers in the same multiblock copolymer. Flipsen Declaration, ¶¶ 18-23.

The Examiner has concluded that Penco teaches the block copolymers of the Applicants’ invention based in part on the synthesis disclosed by Penco in Scheme 1 on page 1740. This synthesis does not disclose that the segments of the copolymer are linked by an aliphatic chain-extender as required by the claims. Dr. Flipsen discusses the synthesis in Scheme 1 and explains how it produces block copolymers with alternating A blocks and B blocks and cannot be used to

produce the Applicants' multiblock copolymers with randomly distributed segments. Flipsen Declaration, ¶¶ 24-25. In particular, Dr. Flipsen states in ¶ 24 that:

I base my finding that Penco teaches block copolymers with alternating A blocks and B blocks on the reaction disclosed by Penco in Scheme 1 on page 1740. Penco et al made multi-block copolymers through reacting a block A (PLGA), which block having an OH group on one end and a carboxylic group on the other end (HO-A-COOH) with a block B (PCDT), which block having on both ends a chloroformate group. It is commonly known to one of ordinary skill in the art that chloroformates react very effectively with protonic groups such as OH and COOH groups. That is the reason why Penco et al modified the PCDT OH end groups to chloroformates, as they want to effectively connect the PCDT blocks to the PLGA blocks forming an AB multi-block copolymer. Those skilled in the art know that a reaction between HO-A-COOH or ClC(=O)O-B-O(O=)CCl themselves will not take place under the reaction conditions shown in Scheme 1 on page 1740.

The Applicants submit that the Declaration of Dr. Flipsen clearly shows that neither Penco nor Cohn teaches or suggests the multiblock copolymers in the claims with randomly distributed segments that are linked using an aliphatic chain-extender. Accordingly, the claims are not obvious in view of the combination of Penco and Cohn and the Applicants respectfully request that the rejection of the claims be withdrawn.

### ***Response to the Advisory Action***

Page 2 of the Advisory Action mailed on July 2, 2009 responds to the arguments submitted in the Applicants' Response to Final Office Action and states that:

Applicants allege that Penco does not teach or suggest a separate PEG chain extender. In response to Applicant's argument that the reference fails to show certain features of Applicant's invention, it is noted that the features upon which applicant relies, (e.g. PEG is not taught as a separate chain-extender) is not recited in the rejected claims.

This statement misconstrues the Applicants' arguments. The Applicants did not argue that: "Penco does not teach or suggest a separate **PEG chain extender**" as the Examiner states, but instead, the Applicants argued at page 7, lines 11-12 of the Response that: "Penco does not teach or suggest block copolymers linked by an **aliphatic chain-extender**." Consequently, the finding that "it is noted that the features upon which applicant relies, (e.g. PEG is not taught as a separate chain-extender) is not recited in the rejected claims" is also incorrect.

Claim 1 clearly states that "the segments [are] linked by a multifunctional chain-extender, wherein said chain-extender is an **aliphatic chain-extender**." This is the "aliphatic chain-extender" that the Applicants argued was neither taught nor suggested by Penco. Dr. Flipsen explains in ¶ 9 of his Declaration that:

Although the abstract and the introduction of Penco mention a chain extension reaction, this involves functionalizing one block (e.g., A) so that it will react with another block (e.g. B). This interpretation is supported by Scheme 1 of Penco, which shows that the polymer chain is built up by a reaction of two macromers. A third reactant for connecting the two macromers is not used.

Accordingly, the claims of the present invention require two different prepolymer segments that are linked by an aliphatic chain-extender that is neither taught nor suggested by Penco.

***Conclusion***

Applicants submit that the Declaration of Dr. Flipsen and the arguments made herein clearly distinguish the cited prior art and respectfully request allowance of the claims.

If the Examiner has any questions relating to this Preliminary Amendment, the Examiner is respectfully invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,

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